

What is claimed is:

1. A method of preparing a vaccine composition, said method comprising the steps of:
 - (A) forming a water-in-oil emulsion comprising
 - (a) water,
 - (b) an alginate,
 - (c) an oil,
 - (d) an antigen, and
 - (e) a surfactant composition comprising at least one of
 - (i) a cellulose ether and at least one nonionic surfactant and
 - (ii) a poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer surfactant and at least one nonionic surfactant;
 - (B) crosslinking the alginate in the emulsion of step (A) with at least two cations selected from the group consisting of aluminum, barium, calcium, lithium, manganese, strontium, and zinc, to form antigen-containing crosslinked alginate microparticles; and
 - (C) harvesting the microparticles of step (B).
 2. The method of claim 1 wherein the microparticles are less than about 10 μm in diameter.
 3. The method of claim 1 wherein the cellulose ether is selected from the group consisting of ethylcellulose, methylcellulose, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and mixtures thereof.
 4. The method of claim 1 wherein a nonionic surfactant is selected from the group consisting of polyoxyethylene surfactants,

anhydrosorbitol ester surfactants, ethoxylated anhydrosorbitol ester surfactants, and mixtures thereof.

5. The method of claim 4 wherein said nonionic surfactant is an alcohol ethoxylate.

6. The method of claim 5 wherein said alcohol ethoxylate is polyoxyethylene (2) oyl ether.

7. The method of claim 4 wherein said nonionic surfactant is an anhydrosorbitol ester.

8. The method of claim 7 wherein said anhydrosorbitol ester is sorbitan trioleate.

9. The method of claim 4 wherein said nonionic surfactant is an ethoxylated anhydrosorbitol ester.

10. The method of claim 9 wherein said ethoxylated anhydrosorbitol ester is polyoxyethylene sorbitan trioleate.

11. The method of claim 1 wherein said a poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer has from about 15 to about 70 propylene oxide residues.

12. The method of claim 11 wherein said poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer has about 30 propylene oxide residues.

13. The method of claim 11 wherein said poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer has the formula $(EO)_3(PO)_{30}(EO)_3$.

14. The method of claim 1 wherein the antigen is selected from the group consisting of live virus, live bacteria, killed virus, killed bacteria, nucleic acids, subunit antigens of infectious agents, and mixtures thereof.

15. The method of claim 1 wherein the cations comprise calcium and zinc.

16. The method of claim 1 wherein said emulsion comprises sources of said cations selected from the group consisting of AlSO_4 , BaCl_2 , CaCl_2 , MnCl_2 , ZnCl_2 , calcium acetate, zinc acetate, strontium nitrate, and mixtures thereof.

17. The method of claim 16 wherein the sources of cations comprise CaCl_2 and ZnCl_2 .

18. The method of claim 16 wherein the sources of cations comprise calcium acetate and zinc acetate.

19. The method of claim 1 wherein the emulsion of step (A) further comprises poly(propylene glycol).

20. The method of claim 1 wherein the emulsion of step (A) comprises a cellulose ether and at least two nonionic surfactants.

21. The method of claim 1 comprising the step of adding at least one nonionic surfactant to the oil.

22. The method of claim 1 comprising the step of coating the microparticles harvested in step (C) with a polymer.

23. The method of claim 22 wherein the polymer is a poly-cation.

24. The method of claim 23 wherein the poly-cation is selected from the group consisting of poly-l-lysine, polyhistidine, polyarginine, polyethyleneimine, and mixtures thereof.

25. The method of claim 24 wherein the poly-cation is poly-l-lysine.

26. The method of claim 1 comprising the step of coating the microparticles harvested in step (C) with a mucosal adjuvant/adhesant.

27. The method of claim 26 wherein the mucosal adjuvant/adhesant is selected from the group consisting of lectins, cholera toxin, B subunit toxin of cholera toxin, recombinant derived subunits of B subunit toxin of cholera toxin, pertussis toxin, heat labile toxin of *E. coli*, exotoxin A of *P. aeruginosa*, and mixtures thereof.

28. The method of claim 1 comprising the step of adding the cations to the emulsion of step (A) in dropwise fashion, while stirring the emulsion at a speed of at least about 1,000 RPM.

29. The method of claim 1 wherein at least one of said nonionic surfactants of steps (A)(e)(i) and (ii) and said poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer has an HLB from about 1 to about 15.

30. The method of claim 1 wherein said nonionic surfactant composition has an HLB of about 8.3.

31. The method of claim 1 wherein the emulsion comprises an anhydrosorbitol ester surfactant and a poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer.

32. The method of claim 31 wherein said ethoxylated anhydrosorbitol ester surfactant comprises polyoxyethylene sorbitan trioleate.

33. The method of claim 32 wherein said poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer has the formula $(EO)_3(PO)_{30}(EO)_3$.

34. The method of claim 33 wherein the emulsion comprises a cellulose ether.

35. A method of preparing a vaccine composition, said method comprising the steps:

- (A) forming a water-in-oil emulsion comprising
 - (a) water,
 - (b) an alginate,
 - (c) an oil,
 - (d) an antigen,
 - (e) methylcellulose, and
 - (f) a surfactant composition comprising polyoxyethylene sorbitan trioleate and a surfactant having the formula $(EO)_3(PO)_{30}(EO)_3$;

(B) crosslinking the alginate in the emulsion of step (A) with zinc acetate and calcium acetate, to form antigen-containing crosslinked alginate microparticles; and

(C) harvesting the microparticles of step (B).

36. A vaccine composition made by the method of any one of claims 1-34.

37. A vaccine composition made by the method of claim 35.

38. A method of vaccinating a vertebrate species comprising the step of administering to said vertebrate species a vaccine composition made by the method of any one of claims 1-34.

39. The method of claim 38 wherein said step of administering said vaccine composition is performed orally.

40. A method of vaccinating a vertebrate species comprising the step of administering to said vertebrate species a vaccine composition made by the method of claim 35.

41. A method of provoking an immune response in a vertebrate species comprising the step of administering to said vertebrate species a vaccine composition made by the method of any one of claims 1-34.

42. A method of provoking an immune response in a vertebrate species comprising the step of administering to said vertebrate species a vaccine composition made by the method of claim 35.